

**This Page Is Inserted by IFW Operations
and is not a part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- **BLACK BORDERS**
- **TEXT CUT OFF AT TOP, BOTTOM OR SIDES**
- **FADED TEXT**
- **ILLEGIBLE TEXT**
- **SKEWED/SLANTED IMAGES**
- **COLORED PHOTOS**
- **BLACK OR VERY BLACK AND WHITE DARK PHOTOS**
- **GRAY SCALE DOCUMENTS**

IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images,
please do not report the images to the
Image Problems Mailbox.**

09095536

* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 14:23:17 ON 02 AUG 2001

=> file medline biosis embase caplus uspatfull

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'MEDLINE' ENTERED AT 14:23:32 ON 02 AUG 2001

FILE 'BIOSIS' ENTERED AT 14:23:32 ON 02 AUG 2001

COPYRIGHT (C) 2001 BIOSIS(R)

FILE 'EMBASE' ENTERED AT 14:23:32 ON 02 AUG 2001

COPYRIGHT (C) 2001 Elsevier Science B.V. All rights reserved.

FILE 'CAPLUS' ENTERED AT 14:23:32 ON 02 AUG 2001

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

COPYRIGHT (C) 2001 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPATFULL' ENTERED AT 14:23:32 ON 02 AUG 2001

CA INDEXING COPYRIGHT (C) 2001 AMERICAN CHEMICAL SOCIETY (ACS)

=> s antibod? (p) tnf (p) il-6

L1 4395 ANTIBOD? (P) TNF (P) IL-6

=> s antibod? (p) tnf (a) il-6

L2 316 ANTIBOD? (P) TNF (A) IL-6

=> s antibod? (s) tnf (a) il-6

L3 269 ANTIBOD? (S) TNF (A) IL-6

=> dup rem l3

PROCESSING COMPLETED FOR L3

L4 118 DUP REM L3 (151 DUPLICATES REMOVED)

=> d l4 ibib kwic

L4 ANSWER 1 OF 118 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 1

ACCESSION NUMBER: 2001:334159 BIOSIS

DOCUMENT NUMBER: PREV200100334159

TITLE: Monoclonal antibody recognizing cell surface antigen CD14.

AUTHOR(S): Adachi, Yoshiyuki (1); Ohno, Naohito; Yadomae, Toshiro
CORPORATE SOURCE: (1) Hachioji Japan

ASSIGNEE: Seikagaku Kogyo Kabushiki Kaisha (Seikagaku Corporation), Tokyo, Japan

PATENT INFORMATION: US 6245897 June 12, 2001

SOURCE: Official Gazette of the United States Patent and Trademark

DOCUMENT TYPE: Patent
LANGUAGE: English

AB A monoclonal **antibody** which recognizes lipopolysaccharide binding site of macrophage cell surface receptor CD14 and has binding activity to monocyte or macrophage cells. The monoclonal **antibody** suppresses the production of an inflammatory mediator such as **TNF**, **IL-6** or **NO** at early stages by recognizing CD14, and competitively inhibiting its binding with LPS. Therefore, it is useful for. . .

=> d his

(FILE 'HOME' ENTERED AT 14:23:17 ON 02 AUG 2001)

FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS, USPATFULL' ENTERED AT 14:23:32 ON 02 AUG 2001

L1 4395 S ANTIBOD? (P) TNF (P) IL-6
L2 316 S ANTIBOD? (P) TNF (A) IL-6
L3 269 S ANTIBOD? (S) TNF (A) IL-6
L4 118 DUP REM L3 (151 DUPLICATES REMOVED)

=> s (tnf (a) antibod?) (p) (il-6 (a) antibod?)

L5 16 (TNF (A) ANTIBOD?) (P) (IL-6 (A) ANTIBOD?)

=> dup rem 15

PROCESSING COMPLETED FOR L5

L6 7 DUP REM L5 (9 DUPLICATES REMOVED)

=> d 16 total ibib kwic

L6 ANSWER 1 OF 7 USPATFULL

ACCESSION NUMBER: 1999:39938 USPATFULL
TITLE: Treatment of autoimmune diseases, including AIDS
INVENTOR(S): Skurkovich, Boris, Pawtucket, RI, United States
Skurkovich, Simon V., Rockville, MD, United States
PATENT ASSIGNEE(S): Advanced Biotherapy Concepts, Inc., Rockville, MD,
United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5888511		19990330
APPLICATION INFO.:	US 1996-771831		19961223 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1993-25408, filed on 26 Feb 1993, now patented, Pat. No. US 5626843		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Scheiner, Toni R.		
LEGAL REPRESENTATIVE:	Panitch Schwarze Jacobs & Nadel, P.C.		
NUMBER OF CLAIMS:	14		
EXEMPLARY CLAIM:	1		
LINE COUNT:	2042		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . treatment is provided comprising exposing the patient's fluid to an immunosorbent comprising an effective amount of antibodies to interleukin, preferably anti-IL-6 **antibody**, in addition to one or more antibodies selected from the group consisting of anti-IFN.alpha., antibody and antibodies to IFN.alpha. receptor, anti-IFN.gamma. antibodies and antibodies to IFN.gamma.

receptor, anti-**TNF antibodies** and antibodies to TNF receptor, and antibodies to an HLA class II antigen or its receptor. This method is particularly. . .

L6 ANSWER 2 OF 7 USPATFULL

ACCESSION NUMBER: 1999:15924 USPATFULL

TITLE: Treatment of vascular leakage and related syndrome such

as septic shock by administration of metalloproteinase inhibitors

INVENTOR(S): Liang, Chi-Ming, Bethesda, MD, United States
Turner, Nancy A., Germantown, MD, United States
Witiak, Donald T., Madison, WI, United States

PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5866570		19990202
APPLICATION INFO.:	US 1994-262888		19940621 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1992-997904, filed on 29 Dec 1992, now abandoned which is a continuation-in-part of Ser. No. US 1992-882855, filed on 14 May 1992, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Scheiner, Toni R.		
ASSISTANT EXAMINER:	Johnson, Nancy A.		
LEGAL REPRESENTATIVE:	DeWitt Ross & Stevens S.C.		
NUMBER OF CLAIMS:	2		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	21 Drawing Figure(s); 14 Drawing Page(s)		
LINE COUNT:	2608		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DRWD FIG. 4 Effect of anti-IL-2 and anti-**TNF antibodies** on the activities of IL-6. Gelatin zymogram evaluation of type IV collagenases in the conditioned medium of THP-1 cells pretreated with the following: (1) none; (2) rIL-6 (25 ng/ml); (3) rIL-6 (25 ng/ml) and anti-**IL-6 antibodies** (200 ng/ml); (4) rTNF (25 ng/ml); (5) rTNF (25 ng/ml)+anti-**IL-6 antibodies** (200 ng/ml); (6) rIL-1 (25 ng/ml); (7) rIL-1 (25 ng/ml)+anti-**IL-6 antibodies** (200 ng/ml); (8) rIL-6 (25 ng/ml)+anti-**TNF antibodies** (10 .mu.g/ml).

DETD . . . or vice versa, THP-1 cells were incubated with either rTNF, rIL-1 or rIL-6 in the presence of anti-TNF, anti-IL-1 or anti-**IL-6 antibodies**. As shown in FIG. 3, the ability of TNF to increase the level of MMP-9 in the cell conditioned medium. .

anti-IL-1 antibodies (lane 4). Similarly, the enhancing effect of IL-1 (lane 5) was decreased by anti-IL-1 (lane 7) but not anti-**TNF antibodies** (lane 6). Anti-TNF or anti-IL-1 antibodies alone had no effect on the release of MMP-9 from THP-1 cells (lanes 8. . . was diminished by anti-IL-6 (FIG. 4 lane 3) but not anti-IL-1 antibodies (data not shown), it was also decreased by anti-**TNF antibodies** (FIG. 4 lane 8). Anti-**IL-6 antibodies** did not interfere with the enhancing effects of TNF (FIG. 4 lanes 4 & 5) or IL-1 (lanes 6 & . . .

L6 ANSWER 3 OF 7 USPATFULL

ACCESSION NUMBER: 1998:42064 USPATFULL

TITLE: Treatment of rheumatoid arthritis with anti-CD4 antibodies in conjunction with anti-TNF antibodies

INVENTOR(S): Feldman, Marc, London, England
Maini, Ravinder N., London, England
Williams, Richard O., London, England

PATENT ASSIGNEE(S): The Kennedy Institute for Rheumatology, London,
England
(non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5741488		19980421
	WO 9408619		19940428
APPLICATION INFO.:	US 1995-403785		19950503 (8)
	WO 1993-GB2070		19931006
			19950503 PCT 371 date
			19950503 PCT 102(e) date

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Feisee, Lila
ASSISTANT EXAMINER: Gambel, Phillip
LEGAL REPRESENTATIVE: Hamilton, Brook, Smith & Reynolds, P.C.
NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT: 680

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD The inflammatory mediators can include agents interfering with TNF, such

as anti-TNF **antibody**, soluble TNF-R (monomeric, IgG fusion proteins, etc.), or blocking peptides and small molecules interfering with TNF receptor signalling or with. . . antagonist, or blocking peptides and small molecules influencing IL-1 synthesis or

IL-1

receptor signalling; agents interfering with IL-6, such as anti-IL-6 **antibody**, anti-gp 130, or blocking peptides and small molecules affecting synthesis or receptor signalling of IL-6; modalities influencing other inflammatory mediators, . . .

L6 ANSWER 4 OF 7 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 96030669 MEDLINE
DOCUMENT NUMBER: 96030669 PubMed ID: 7558150
TITLE: Interaction of interleukin-6, tumour necrosis factor and interleukin-1 during Listeria infection.
AUTHOR: Liu Z; Simpson R J; Cheers C
CORPORATE SOURCE: Department of Microbiology, University of Melbourne, Victoria, Australia.
SOURCE: IMMUNOLOGY, (1995 Aug) 85 (4) 562-7.
JOURNAL CODE: GH7; 0374672. ISSN: 0019-2805.
PUB. COUNTRY: ENGLAND: United Kingdom
JOURNAL; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199511
ENTRY DATE: Entered STN: 19951227
Last Updated on STN: 19951227
Entered Medline: 19951120

AB . . . cytokines during infection. Treatment with recombinant (r)IL-6 enhanced TNF production by spleen cells during the first 2 days of infection. Anti-TNF **antibody** could totally abolish the protective effect of rIL-6, while the optimal protective function of TNF could not be achieved when IL-6 was neutralized by anti-IL-6 **antibody**. IL-1 induced a high level of IL-6 in the serum a short time after its administration, and neutralization of IL-6.

L6 ANSWER 5 OF 7 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 93178361 MEDLINE
DOCUMENT NUMBER: 93178361 PubMed ID: 8382602
TITLE: Synergistic roles of interleukin-6, interleukin-1, and tumor necrosis factor in the adrenocorticotropin response

to bacterial lipopolysaccharide in vivo.
 AUTHOR: Perlstein R S; Whitnall M H; Abrams J S; Mougey E H; Neta R
 CORPORATE SOURCE: Department of Experimental Hematology, Armed Forces Radiobiology Research Institute, Bethesda, Maryland 20889-5145.
 SOURCE: ENDOCRINOLOGY, (1993 Mar) 132 (3) 946-52.
 Journal code: EGZ; 0375040. ISSN: 0013-7227.
 PUB. COUNTRY: United States
 Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
 ENTRY MONTH: 199304
 ENTRY DATE: Entered STN: 19930416
 Last Updated on STN: 19970203
 Entered Medline: 19930401

AB . . . course of LPS-induced ACTH release, we used blocking antibodies to IL-6, TNF, and the IL-1 receptor. Our results demonstrate that anti-**IL-6 antibody** abrogated ACTH induction throughout the course of the response both 2 and 4 h after LPS challenge. In contrast, anti-IL-1 receptor and anti-**TNF antibody**, given individually, blocked ACTH production at 4 h, but not at 2 h. Only combined administration of these two antibodies. . .

L6 ANSWER 6 OF 7 MEDLINE DUPLICATE 3
 ACCESSION NUMBER: 94007268 MEDLINE
 DOCUMENT NUMBER: 94007268 PubMed ID: 7691450
 TITLE: Modulation of adhesion molecule expression on endothelial cells during the late asthmatic reaction: role of macrophage-derived tumour necrosis factor-alpha.
 AUTHOR: Lassalle P; Gosset P; Delneste Y; Tsicopoulos A; Capron A; Joseph M; Tonnel A B
 CORPORATE SOURCE: INSERM CJF no. 90-06, Institut Pasteur, Lille, France.
 SOURCE: CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (1993 Oct) 94 (1) 105-10.
 Journal code: DD7; 0057202. ISSN: 0009-9104.
 PUB. COUNTRY: ENGLAND: United Kingdom
 Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199311
 ENTRY DATE: Entered STN: 19940117
 Last Updated on STN: 19960129
 Entered Medline: 19931109

AB . . . ICAM-1 ($r = 0.80$, $P < 10(-4)$) and ELAM-1 expression ($r = 0.88$, $P < 10(-5)$); and (ii) a neutralizing anti-**TNF antibody** decreased their effect (68% and 80% respectively on ICAM-1 and ELAM-1 expression). Moreover, the role of IL-6 was excluded on. . . the basis both of the hrIL-6 inefficiency to induce ICAM-1 and ELAM-1 synthesis, even in costimulation with hrTNF, and of anti-**IL-6 antibody** to neutralize the effect of AM supernatants. Our results suggest that, beside mast cells and lymphocytes, macrophages might participate in. . .

L6 ANSWER 7 OF 7 USPATFULL
 ACCESSION NUMBER: 92:63944 USPATFULL
 TITLE: TNF-inhibitory protein and a method of production
 INVENTOR(S): Dembinski, Wlodzimierz E., Buffalo, NY, United States
 Ip, Margot, Orchard Park, NY, United States
 PATENT ASSIGNEE(S): Health Research, Inc., Buffalo, NY, United States
 (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5136021		19920804

APPLICATION INFO.: US 1990-486044 19900227 (7)
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Lacey, David L.
ASSISTANT EXAMINER: Guest, Shelly J.
LEGAL REPRESENTATIVE: Pennie & Edmonds
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Figure(s); 2 Drawing Page(s)
LINE COUNT: 768

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . present invention is 28 kDa as described above. Further, the activity of the TNF-inhibitory protein is not neutralized by an anti-TNF antibody, an anti-IL-1 antibody or an anti-IL-6 antibody.

=> log y

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	38.34	38.55

STN INTERNATIONAL LOGOFF AT 14:28:18 ON 02 AUG 2001